Amendments to the Specification:

Please replace the paragraph beginning at page 19, line 26 with the following amended paragraph:

A "chemotherapeutic agent" is a chemical compound useful in the treatment of cancer. Examples of chemotherapeutic agents include adriamycin, doxorubicin, epirubicin, 5-fluorouracil, cytosine arabinoside ("Ara-C"), cyclophosphamide, thiotepa, busulfan, cytoxin, taxoids, *e.g.*, paclitaxel (~~Taxol~~TAXOL®, Bristol-Myers Squibb Oncology, Princeton, NJ), and doxetaxel (~~Taxotere~~TAXOTERE®, Rhône-Poulenc Rorer, Antony, Rnace), toxotere, methotrexate, cisplatin, melphalan, vinblastine, bleomycin, etoposide, ifosfamide, mitomycin C, mitroxantrone, vincristine, vinorelbine, carboplatin, teniposide, daunomycin, carminomycin, aminopterin, dactinomycin, mitomycins, esperamicins (see U.S. Pat. No. 4,675,187), 5-FU, 6-thioguanine, 6-mercaptopurine, actinomycin D, VP-16, chlorambucil, melphalan, and other related nitrogen mustards. Also included in this definition are hormonal agents that act to regulate or inhibit hormone action on tumors such as tamoxifen and onapristone.

Please replace the paragraph beginning at page 25, line 20 with the following amended paragraph:

Although the PCR step can use a variety of thermostable DNA-dependent DNA polymerases, it typically employs the Taq DNA polymerase, which as a 5'-3' nuclease activity but lacks a 3'-5' proofreading endonuclease activity. Thus ~~TaqMan~~TaqMan® PCR typically utilizes the 5'-nuclease activity of Taq or Tth polymerase to hydrolyze a hybridization probe bound to its target amplicon, but any enzyme with equivalent 5' nuclease activity can be used. Two oligonucleotide primers are used to generate an amplicon typical of a PCR reaction. A third oligonucleotide, or probe, is designed to detect nucleotide sequence located between the two PCR primers. The probe is non-extendible by Taq DNA polymerase enzyme, and is labeled with a reporter fluorescent dye and a quencher fluorescent dye. Any laser-induced emission from the reporter dye is quenched by the quenching dye when the two dyes are located close together as they are on the probe. During the amplification reaction, the Taq DNA polymerase enzyme cleaves the probe in a template-dependent manner. The resultant probe fragments disassociate in solution, and signal from the released reporter dye is free from the quenching effect of the

second fluorophore. One molecule of reporter dye is liberated for each new molecule synthesized, and detection of the unquenched reporter dye provides the basis for quantitative interpretation of the data.

Please replace the paragraph beginning at page 25, line 34 with the following amended paragraph:

~~TaqMan~~TaqMan® RT-PCR can be performed using commercially available equipments, such as, for example, ~~ABI PRIZM 7700™~~ ABI PRIZM® 7700 Sequence Detection ~~System™~~ System (Perkin-Elmer-Applied Biosystems, Foster City, CA, USA), or ~~Lightcycler~~LIGHTCYCLER® (Roche Molecular Biochemicals, Mannheim, Germany). In a preferred embodiment, the 5' nuclease procedure is run on a real-time quantitative PCR device such as the ~~ABI PRIZM 7700™~~ ABI PRIZM® 7700 Sequence Detection ~~System™~~ System. The system consists of a thermocycler, laser, charge-coupled device (CCD), camera and computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the CCD. The system includes software for running the instrument and for analyzing the data.

Please replace the paragraph beginning at page 27, line 18 with the following amended paragraph:

Regardless of the method chosen for gene expression profiling, and to quantify mRNA transcription, the ~~crust~~ crux of the present invention is the identification of genes the expression of which is selectively enhanced by retinoid treatment in cancer cells driven by Wnt signaling, relative to normal cells. In particular, the gene expression profile of tumor cells characterized by the involvement of the Wnt signaling pathway is determined in the presence and absence of Wnt, e.g. Wnt-1 expression, and in the presence and absence of retinoid treatment. After quantitation of the gene expression data, genes are identified, the expression of which is selectively upregulated by retinoid treatment of Wnt-expressing tumor cells, relative to normal cells treated with the same retinoid, and, preferably, also relative to tumor cells not expressing Wnt, with or without retinoid treatment. As discussed before, the retinoid may be a retinoic acid (also known as tretinoin, vitamin A acid or vitamin A1), including both all-trans-retinoic acid (all-trans-RA)

and 9-cis-retinoic acid (9-cis-RA), and retinoic acid derivatives consisting of four isoprenoid units joined in a head-to-tail manner, such as retinol, retinal, substituted retinoids, seco-, nor-, and retro-retinoids. All retinoids may be formally derived from a monocyclic parent compound containing five carbon-carbon double bonds and a functional group at the terminus of the acyclic portion.

Please replace the paragraph beginning at page 47, line 30 with the following amended paragraph:

Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by [[ATCC]]ATCC® accession numbers is the American Type Culture ~~Collection~~Collection®, Manassas, VA. In the following Examples, unless otherwise specified, "Sra6" will refer to native sequence PRO10282 polypeptide.

Please replace the paragraph beginning at page 52, line 3 with the following amended paragraph:

For purification, *E. coli* pastes (6-10 gm pellets) were resuspended in 10 volumes (w/v) of 7 M guanidine HCl, 20 mM Tris, pH 8, buffer. Solid sodium sulfite and sodium tetrathionate were added to make final concentrations of 0.1 M and 0.02 M, respectively, and the solution was stirred overnight at 4°C. The solution was clarified by centrifugation and loaded onto a ~~Qiagen~~QIAGEN® Ni-NTA metal chelate column equilibrated in 6 M guanidine, HCl, 20 mM Tris, pH 7.4. The column was washed with additional buffer containing 50 mM imidazole (~~Calbiochem~~CALBIOCHEM®, Utrol grade). The protein was eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein were pooled, dialyzed against 1 mM HCl and store at 4°C.

Please replace the paragraph beginning at page 52, line 21 with the following amended paragraph:

In one embodiment, the selected host cells may be 293 cells. Human 293 cells ([[ATCC]]ATCC® CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or

antibiotics. About 10 μg pRK5-PRO10282 or pRK5-PRO19578 DNA is mixed with about 1 μg DNA encoding the VA RNA gene [Thimmappaya et al., Cell, 31:543 (1982)] and dissolved in 500 μl of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M $CaCl_2$. To this mixture is added, dropwise, 500 μl of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM $NaPO_4$, and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Please replace the paragraph beginning at page 54, line 5 with the following amended paragraph:

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect® (~~Qiagen~~QIAGEN®), Dosper® or Fugene® (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately 3×10^{-7} cells are frozen in an ampoule for further growth and production as described below.

Please replace the paragraph beginning at page 61, line 33 with the following amended paragraph:

Real-time quantitative PCR (RT-PCR, for example, ~~TAQMAN ABI PRIZM 7700™ Sequence Detection System™~~TaqMan® ABI PRIZM® 7700 Sequence Detection System [Perkin Elmer, Applied Biosystems Division, Foster City, California]), was used to monitor quantitative differences in the level of expression of the PRO10292 (Stra6) encoding gene (corresponding to DNA148380-2827) in normal cells and cells derived from certain cancers or cancer cell lines, using ~~Taqman~~TaqMan® assay reagents. 50 μl RT-PCR reactions consisted of 5 μl 10x ~~Taqman~~TaqMan® Buffer A, 300 μM of each dNTF, 5 mM $MgCl_2$, 10 units of RNAse inhibitor, 12.5 units ~~ofMuLV~~of MuLV Reverse Transcriptase, 1.25 units of ~~AmpliTaq Gold~~AmpliTaq Gold® DNA Polymerase, 200 nM probe, 500 nM primers and 100 ng RNA. Reaction conditions consisted of reverse transcription at 48°C for 30 minutes, denaturation at 95°C for 25 seconds and 65°C for one minute. Reaction products were analyzed on 4-20% polyacrylamide gels (Novex).

Please replace the paragraph beginning at page 63, line 25 with the following amended paragraph:

RNA was prepared from the foregoing cultured cell lines. The isolation was performed using purification kit, buffer set and protease from ~~Qiagen~~QIAGEN®, according to the manufacturer's instructions and the description below. More specifically, total RNA from cells in culture was isolated using ~~Qiagen RNeasy~~QIAGEN RNeasy® midi-columns. Total RNA from tissue samples was isolated using RNA Stat-60 (Tel-Test). RNA prepared from tumor was isolated by cesium chloride density gradient centrifugation.

Please replace the paragraph beginning at page 64, line 4 with the following amended paragraph:

~~Quiagen~~QIAGEN® protease (prepared as indicated above, 1.0 ml) was added, followed by vortexing and incubation at 50°C for 3 hours. The incubation and centrifugation were repeated until the lysates were clear (e.g., incubating additional 30-60 minutes, pelleting at 3000 x g for 10 minutes, 4°C).

Please replace the paragraph beginning at page 64, line 9 with the following amended paragraph:

The results obtained from the real-time PCR analysis of RNA were initially expressed as delta CT units. One unit corresponds to one PCR cycle or approximately a 2-fold amplification relative to normal, two units correspond to 4-fold, 3 units to 8-fold amplification and so on. The data is converted to fold difference and presented as such. Initially, reverse transcriptase was used to synthesize cDNA from 100 ng total RNA or polyA+ RNA using oligo(dT) as a primer. The resultant cDNA was then used as a template for PCR. Quantitation was obtained using primers derived from the 3'-untranslated regions of the PRO10282 encoding sequence and a ~~TAQMAN™~~TaqMan® fluorescent probe corresponding to the respective intervening sequences. Using the 3' region tends to avoid crossing intron-exon boundaries in the genomic DNA, an essential requirement for accurate assessment of RNA expression using this method. The sequences for the primers and probes (forward, reverse, and probe) using for the PRO10282 encoding gene amplification were as follows:

Please replace the paragraph beginning at page 65, line 7 with the following amended paragraph:

As noted above, the 5' nuclease procedure is run on a real-time quantitative PCR device such as the ~~ABI PRIZM 7700™~~ ABI PRIZM® 7700 Sequence Detection ~~System™~~ System. The system consists of a ~~thermocyler~~thermocycler, laser, charge-coupled device (CCD), camera and computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the CCD. The system includes software for running the instrument and for analyzing the data.

Please replace the paragraph beginning at page 73, line 2 with the following amended paragraph:

Confirmation of gene expression was performed using quantitative RT-PCR using ~~Taqman~~TaqMan® assay reagents in an [[ABI]] ABI PRIZM® 7700 Sequence Detector from Perkin-Elmer, Applied Biosystems. RT-PCR reactions consisted of 100 ng RNA, 5 µl 10x ~~Taqman~~TaqMan® Buffer A, 300 µM of each dNTP, 5 mM $MgCl_2$, 10 units of RNase inhibitor, 12.5 units of MuLV Reverse Transcriptase, 1.25 units of ~~AmpliTaq Gold~~AmpliTaq Gold® DNA Polymerase, 200 nM probe, and 500 nM primers. Reaction conditions consisted of reverse transcription at 48°C for 30 minutes, denaturation at 95°C for 10 minutes, and 40 cycles of 95°C for 25 seconds and 65°C for 1 minute. Reaction products were anlayzed on 4-20 polyacrylamide gels.

Please replace the paragraph beginning at page 73, line 36 with the following amended paragraph:

To determine RAR-dependent transactivation, Cos-7 cells were cotransfected with the indicated expression plasmids and the TREpall luciferase reporter construct (Beyers) using ~~Effectene~~EFFECTENE® (~~Qiagen~~QIAGEN®) transfection reagent per the manufacturer's instructions. Expression plasmids have been described elsewhere. Cells were treated with 1µM ATRA or DMSO control on the day of transfection and harvested 72 hours later by lysis in Triton X-100 lysis buffer. Luciferase activity in 10 µl of lysate was analyzed using a Tropix

TR717 microplate luminometer. Activity was normalized to Renilla luciferase activity produced by cotransfection with SV40-Renilla luciferase. Activation of LEF/TCF-dependent transcription was determined by cotransfection with indicated plasmids and Top-tk-luciferase plasmid. Activity was determined as described above.

Please replace the paragraph beginning at page 74, line 10 with the following amended paragraph:

The murine C57MG breast epithelial cell line undergoes morphological transformation in response to the expression of various Wnt genes (Wong *et al., Mol Cell Biol* 14:6278-6286 (1994)). A version of this cell line that was engineered to conditionally express Wnt-1 in response to the removal of tetracycline from the culture medium was employed for the gene expression profiling experiments. To identify genes that were preferentially activated by the combination of retinoic acid and Wnt-1 signaling, four different conditions were established for the treatment of cells. As a control, cells were left in medium containing tetracycline plus DMSO, the vehicle for retinoic acid. A second dish of cells was treated with 100nM all-*trans*-retinoic acid (ATRA) in the presence of tetracycline, while a third dish of cells received DMSO control and the tetracycline was removed to activate expression of Wnt-1. Finally, a fourth dish of cells was treated with ATRA and the tetracycline was removed. Following a forty eight hour incubation period, cells were harvested and RNA was extracted and purified. Probes synthesized from the RNA was hybridized to the ~~Affymetrix Mouse Gene Chip~~Affymetrix® Mouse GeneChip® "A" Mu74 containing 12,000 oligonucleotide probe sets. The experiment, as initiated from the growth and treatment of cells, was performed three independent times. Data is presented for mRNA transcripts that underwent at least a two-fold increase or a 50% decrease relative to the untreated cells in all three experiments. In addition, a time course was performed in which RNA was collected from treated cells at 24, 48 and 72 hours. These data are included only for select genes.

Please replace the paragraph beginning at page 80, line 2 with the following amended paragraph:

The following materials have been deposited with the American Type Culture ~~Collection~~Collection®, 10801 University Blvd., Manassas, VA 20110-2209, USA ~~(ATCC)~~ATCC®:

Material	[[ATCC]]ATCC® Dep. No.	Deposit Date
DNA148380-2827	PTA-1181	January 11, 2000
DNA148389-2827-1	PTA-1402	February 23, 2000

Please replace the paragraph beginning at page 80, line 8 with the following amended paragraph:

These deposits were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorgansims for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposit will be made available by [[ATCC]]ATCC® under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and [[ATCC]]ATCC®, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 U.S.C. § 122 and the Commissioner's rules pursuant thereto (including 37 C.F.R. § 1.14 with particular reference to 886 OG 638).